Group VI, claim(s) 1-5 and 14-16, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a oxazocine ring.

Group VII, claim(s) 7-8 and 14-41, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a morpholine ring.

Applicant hereby elects the claims of Group II, claim(s) 1-40, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a piperidine ring for continued prosecution.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

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PATENT
ATTORNEY DOCKET
NO. 64978

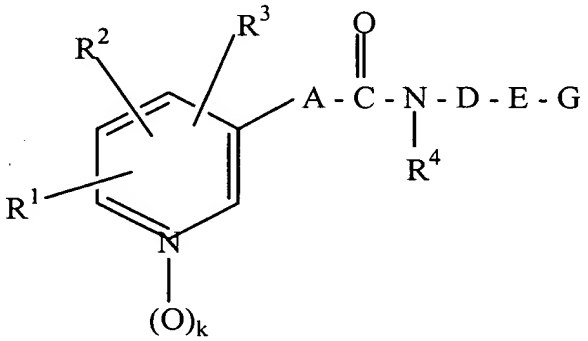
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Biedermann et al.
Serial No.: 09/242,540
Filed: February 18, 1999
Title: PYRIDYL ALKENE AND PYRIDYL ALKINE-ACID AMIDES AS CYTOSTATICS AND IMMUNOSUPPRESSIVES
Group Art Unit: 1624
Examiner: B. Coleman

Version with Markings to Show Changes Made

Honorable Commissioner of Patents
and Trademarks
ATTENTION: Assistant Commissioner
for Patents
Washington, D.C. 20231

42. (once amended) A compound of formula (I) **and pharmaceutically acceptable salts of formula (I)**



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, C_1-C_4-hydroxyalkyl, hydroxy, C_1-C_4-alkoxy, benzyloxy, [C_1] C_2-C_4-alkanoyloxy, C_1-C_4-alkylthio, C_2-C_5-alkoxycarbonyl, aminocarbonyl, C_3-C_9-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, [and] NR^5R^6, and bridged R^1R^2 wherein

R^5 is selected from the group consisting of hydrogen and C_1-C_6-alkyl; [,] and

R^6 is [are selected independently from each other] selected from the group consisting of hydrogen and C_1-C_6-alkyl; [,]

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6-alkyl, trifluoromethyl and hydroxy and bridged R^1R^2;

wherein

[R^1 and R^2, in the case they] bridged R^1R^2 is where R^1R^2 are adjacent[, optionally] and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; [,] wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6-alkyl; and

R^8 [are, independent from each other,] is selected from the group consisting of hydrogen [or] and C_1-C_6-alkyl; [,]

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6-alkyl; [,]

R^4 is selected from the group consisting of hydrogen, C_1-

C_6-alkyl, C_3-C_6-alkenyl, hydroxy, C_1-C_6-alkoxy and benzyloxy; [,]

k is 0 or 1,

A is selected from **the group consisting of** C_2-C_6-alkenylene, [which is optionally]

a substituted C_2-C_6-alkenylene which is substituted one to three-fold by C_1-C_3-alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6-alkadienylene, [which is optionally]

a substituted C_4-C_6-alkadienylene which is substituted once or twice by C_1-C_3-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene, [which is optionally]

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3-alkyl, fluorine, or cyano, and ethinylene; [,]

D is selected from **the group consisting of**

C_1-C_{10}-alkylene, [optionally]

a substituted C_1-C_{10}-alkylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

C_2-C_{10}-alkenylene, [optionally]

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy, wherein the double bond [optionally] is to [ring] E,

C_3-C_{10}-alkinylene, [optionally]

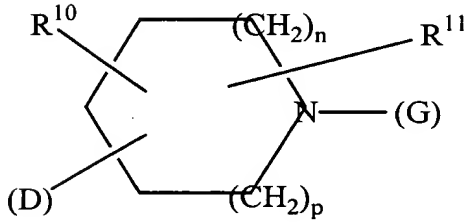
a substitued C_3-C_{10}-alkinylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy, [and]

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1-C_{10}-alkylene, C_2-C_{10}-alkenylene and C_3-C_{10}-alkinylene, [wherein] **the isosterically replaced C_1 to**

C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR^9, CO, SO or SO_2; [,] wherein

R^9 is selected from the group consisting of hydrogen, C_1-C_3-alkyl, C_2-C_6-acyl and methanesulfonyl; [,]

E is



[(E1)],

wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, or 3, [with the proviso that] wherein **n** + **p** [= 2] ≤ 3,

R^{10} is selected from the group consisting of hydrogen, C_1-C_3-alkyl, hydroxy, hydroxymethyl, carboxy and C_2-C_7-alkoxycarbonyl; [,]

R^{11} is selected from the group consisting of hydrogen [or] and an oxo group adjacent to the nitrogen atom in E; [,]

G is selected from **the group consisting of** hydrogen, **G1**, **G2**, **G3**, **G4** and **G5**[,] wherein

G1 [represents the residue] **is** $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$ [(G1)] wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from **the group consisting of**
hydrogen,
C_1-C_6-alkyl,
C_3-C_6-alkenyl,
C_3-C_6-alkinyl,
C_3-C_8-cycloalkyl,
benzyl,
phenyl,
monocyclic aromatic five- and six-membered heterocycles[,] which **heterocycles** contain one to three hetero-atoms selected from **the group consisting of** N, S and O, [and are the N, S and O being] **which heterocycles are** either bound directly **to** or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system[s] with 8 to 16 ring atoms and at least one aromatic ring[, wherein the bond occurs] **and the carbocyclic ring and aromatic ring being bonded with a bond which is** either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16

ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and **the carbocyclic ring and aromatic ring being bonded with a bond which is** [the bond occurs] either over an aromatic or a hydrogenated ring, and either directly or over a methylene group[,];

R^{13} has the same meaning as R^{12}, but is selected independently thereof,

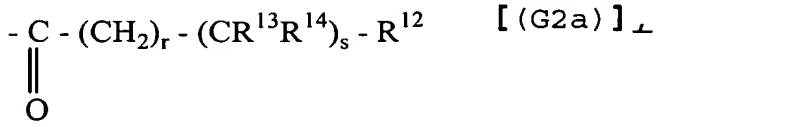
R^{14} is selected from **the group consisting of** hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,
monocyclic aromatic five- and six-membered heterocycles[,] which contain one to three hetero-atoms selected from **the group consisting of** N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system[s] with 8 to 16 ring atoms and at least one aromatic ring[, wherein the bond occurs] **and the carbocyclic ring and the aromatic ring being bonded with a bond which is** either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system[s] with 8 to 16 ring atoms and at least one aromatic ring, [wherein] **which heterocycles contain** one to three ring atoms are selected from **N,** S and O and the **heterocyclic ring and aromatic ring being bonded with a bond which is** [bond occurs either] over an aromatic or a hydrogenated ring and either directly or over a

methylene group[,]

G2 is selected from **the group consisting of**



[(G2a)],

[and]

[(G2b)],

and

---

wherein R^{12} and R^{14} have the above meaning, **and Q** [or the group

] is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

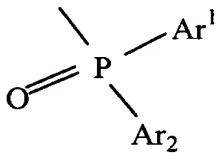
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from [the] **an** essential nitrogen atom[, optionally] contain one or two further hetero-atoms selected from N, S and O, [and the group consisting of]

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms**, and**

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from [the] **an** essential nitrogen atom[, optionally] contain one or two further hetero-atoms selected from N, S and O,

G3 is [the residue] $-SO_2-(CH_2)_r-R^{12}$ [(G3)],

G4 is [the residue]



[(G4)],

wherein

Ar^1 **is selected from the group consisting of phenyl, pridyl and naphthyl;** and

Ar^2 [are selected independently of each other] **is selected** from **the group consisting of** phenyl, pyridyl and naphthyl;[,]

G5 is [the residue] $-COR^{15}$ [(G5)],

wherein

R^{15} is selected from **the group consisting of** trifluoromethyl, C_1-C_6-alkoxy, C_3-C_6-alkenyloxy and benzyloxy;[,] **and**

wherein aromatic [ring systems] **rings** in [the substituents] **R^1**, [**R^2**,] **R^4**, **R^{12}**, **R^{13}**, **R^{14}**, **R^{15}**, **Q**, **Ar^1** and **Ar^2** [and in the ring system **$-NR^{12}R^{14}$** optionally carry independently of

each other] **are unsubstituted or substituted, the substituted rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 having** one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, **and a substituted C_1-C_6-alkoxy** which is [optionally] entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups of [the] **an** aromatic ring **in the substituted C1-C6 alkoxy** [or ring system optionally] **may** form an additional ring over a methylenedioxy bridge, [stereoisomers and/or mixtures thereof and pharmacologically acceptable acid addition salts with the exception of] wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide [hydrochloride].

43. (once amended) A compound according to claim 42, wherein:

R^1 is selected from **the group consisting of** hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, C_1-C_4-alkoxy, ethylthio, methoxycarbonyl, tert-butoxycarbonyl, aminocarbonyl, carboxy, and phenoxy,

R^2 is selected from **the group consisting of** hydrogen, halogen, trifluoromethyl and hydroxy,

R^3 is hydrogen or halogen,

R^4 is selected from **the group consisting of** hydrogen, C_1-C_3-alkyl, hydroxy and C_1-C_3-alkoxy,

k is 0 or 1,

A is selected from **the group consisting of** C_2-C_6-alkenylene, [optionally]

a substituted **C_2-C_6-alkenylene which is substituted** once or twice by C_1-C_3-alkyl, hydroxy or fluorine,

a C_4-C_6-alkadienylene, [optionally]

a substituted **C_4-C_6-alkadienylene which is substituted** by C_1-C_3-alkyl or by 1 or 2 fluorine atoms, [and]

1,3,5-hexatrienylene, [optionally] **and**

a substituted **1,3,5-hexatrienylene which is substituted** by fluorine,

D is selected from **the group consisting of** C_1-C_8-alkylene, [optionally]

a substituted **C_1-C_8-alkylene which is substituted** once or twice by methyl or hydroxy,

C_2-C_8-alkenylene, [optionally]

a substituted **C_2-C_8-alkenylene which is substituted** once or twice by methyl or hydroxy,

an E double bonded substituted C_2-C_8-alkenylene which has a double bond [wherein the double bond optionally is] to ring E,

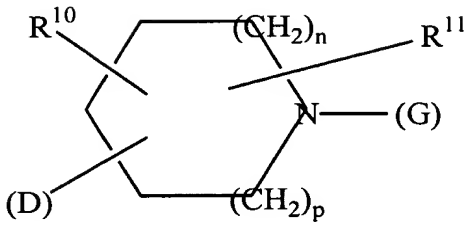
C_3-C_8-alkinylene, [optionally]

a substituted **C_3-C_8-alkinylene which is substituted** once or twice by methyl or hydroxy, and

an isosterically replaced C1 to C8 group selected from the group consisting of C_1-C_8-alkylene, C_2-C_8-alkenylene and C_3-C_8-alkinylene, **the isosterically replaced C1 to C8 group having methylene units and** [in which] one to three methylene units are isosterically replaced by O, S, NH, $N(CH_3)$,

$N(COCH_3)$, $N(SO_2CH_3)$, CO, SO or SO_2,

E is



wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, **or 3,** [with the proviso that] **wherein** **n** + **p** [= 2] ≤ **3**,

R^{10} is selected from **the group consisting of** hydrogen, C_1-C_3-alkyl, hydroxy, hydroxymethyl, carboxy and C_2-C_7-alkoxycarbonyl**;** [,]

R^{11} is **selected from the group consisting of** hydrogen [or] **and** an oxo group adjacent to the nitrogen atom **in E;** [,]

G is selected from **the group consisting of** hydrogen, **G1**, **G2**, **G3**, **G4** and **G5;** [,] wherein

G1 [represents the residue] **is** $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$ [(G1)] wherein

r is 0, 1 or 2, and
s is 0 or 1,

R^{12} is selected from **the group consisting of** hydrogen, C_1-C_6-alkyl, C_3-C_8-cycloalkyl, benzyl, phenyl, [the group consisting of] benzocyclobutyl, indanyl, indenyl, oxoindanyl, naphthyl,

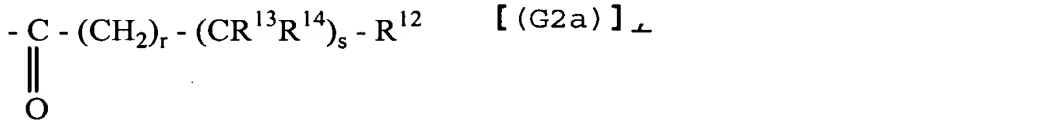
dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, biphenylenyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, phenanthryl, dihydrophenanthryl, oxodihydrophenanthryl, dibenzocycloheptenyl, oxodibenzocycloheptenyl, dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl, dihydrodibenzocyclooctenyl, tetrahydrodibenzocyclooctenyl and oxotetrahydrodibenzocyclooctenyl, bound directly or over a methylene group, [and the group consisting of] furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl, dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolinyl, benzisoxazolyl, oxobenzisoxazolinyl, benzothiazolyl, oxobenzthiazolinyl, benzoisothiazolyl, oxobenzoisothiazolinyl, benzimidazolyl, oxobenzimidazolinyl, indazolyl, oxoindazolinyl, benzofurazanyl, benzothiadiazolyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl, pyrazolopyridyl, oxodihydropyrazolopyridyl, thienopyrimidinyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, dihydroquinolyl, oxodihydroquinolinyl, tetrahydroquinolyl, oxotetrahydroquinolinyl, benzodioxanyl, quinoxalinyl, quinazolinyl, naphthyridinyl, carbazolyl, tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, oxodihydrodibenzoxepinyl, benzocycloheptathienyl, oxobenzocycloheptathienyl, dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, octahydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl,

benzocycloheptapyridyl, oxobenzocycloheptapyridyl, dihydropyridobenzodiazepinyl, dihydrodibenzoxazepinyl, dihydropyridobenzoxepinyl, dihydropyridobenzoxazepinyl, oxodihydropyridobenzoxazepinyl, dihydrodibenzothiazepinyl, oxodihydrodibenzothiazepinyl, dihydropyridobenzothiazepinyl, and oxodihydropyridobenzothiazepinyl, bound directly or over a methylene group,

R^{13} has the same meaning as R^{12}, but is selected independently therefrom,

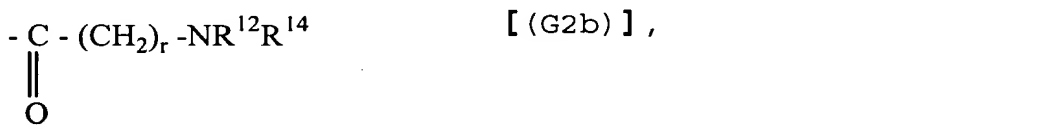
R^{14} is selected from **the group consisting of** hydrogen, hydroxy, methyl, benzyl, phenyl, [and, the group consisting of] indanyl, indenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl, and tetrahydroquinolyl, bound directly or over a methylene group,

G2 is selected from [the residues] **the group consisting of**



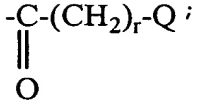
[(G2a)],

[and]



[(G2b)],

and



wherein R^{12} and R^{14} have the above meaning, **and Q** [or the group

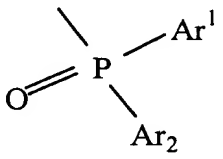
$-NR^{12}R^{14}$]

is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of azetidine, pyrrolidine, piperidine, (1H)tetrahydropyridine, hexahydroazepine, (1H)tetrahydroazepine, octahydroazocine, pyrazolidine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, thiomorpholine, thiomorpholine-1,1-dioxide, 5-aza-bicyclo[2.1.1]hexane, 2-aza-bicyclo[2.2.1]heptane, 7-aza-bicyclo[2.2.1]heptane, 2,5-diaza-bicyclo[2.2.1]heptane, 2-aza-bicyclo[2.2.2]octane, 8-aza-bicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, 9-azabicyclo[3.3.1]nonane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[c]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (10H)-phenoxazine, (10H)-phenothiazine, (5H)-dibenzazepine, (5H)-dihydrodibenzazepine, (5H)-octahydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-

dihydrodibenzo[b,f]oxazepine, (10H)-dihydrodibenzo[b,f]thiazepine, and (5H)-tetrahydrodibenzazocine,

G3 is $-SO_2-(CH_2)_r-R^{12}$ [(G3)],

G4 is



[(G4)],

wherein

Ar^1 and

Ar^2 are selected independently of each other from **the group consisting of** phenyl, pyridyl and naphthyl; [,]

G5 is $-COR^{15}$ [(G5)],

wherein

R^{15} is selected from **the group consisting of** trifluoromethyl, C_1-C_6-alkoxy, C_3-C_6-alkenyloxy and benzyloxy; [,] **and**

wherein aromatic [ring systems optionally] **rings** are substituted **or unsubstituted** independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, **and a substituted** C_1-C_6-alkoxy **which is** entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl,

benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups [in the ring] **of an aromatic ring in the substituted C1-C6 alkoxy** [or ring system optionally] **may** form an additional ring over a methylenedioxy bridge.

44. (once amended) A compound according to claim 43 wherein:

R^1 is selected from **the group consisting of** hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, methoxy and methoxycarbonyl,

R^2 is hydrogen or halogen,

R^3 is hydrogen,

R^4 is selected from **the group consisting of** hydrogen, C_1-C_3-alkyl and hydroxy,

k is 0 or 1,

A is selected from **the group consisting of** C_2-C_6-alkenylene, [optionally]

a substituted **C_2-C_6-alkenylene which is substituted** once or twice by hydroxy or fluorine, [or]

C_4-C_6-alkadienylene, [optionally]

a substituted **C_4-C_6-alkadienylene which is substituted** by one or two fluorine atoms, and

1,3,5-hexatrienylene

D is selected from **the group consisting of** C_2-C_8-alkylene,

[optionally]

a substituted C_2-C_8-alkylene which is substituted by methyl or hydroxy

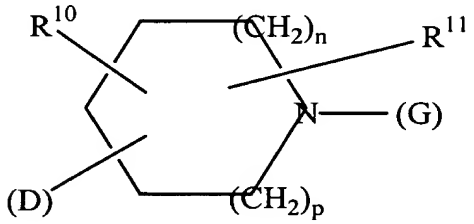
C_2-C_8-alkenylene, [optionally]

a substituted C_2-C_8-alkenylene which is substituted by methyl or hydroxy, [wherein the double bond optionally is to ring E, and]

a substituted C_2-C_8-alkenylene which is substituted by methyl or hydroxy, wherein the double bond is to ring E, [and]

an isosterically replaced C2 to C8 group selected from the group consisting of C_2-C_8-alkylene and C_2-C_8-alkenylene, [wherein] the isosterically replaced C2 to C8 group having methylene units and one to three of the methylene units are isosterically replaced by O, NH, $N(CH_3)$, $N(COCH_3)$, $N(SO_2CH_3)$ or CO,

E is



wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, or 3, [with the proviso that] wherein **n + p** [= 2] ≤ 3,

R^{10} is selected from the group consisting of hydrogen, methyl and hydroxyl,

R^{11} is hydrogen or an oxo group adjacent to the nitrogen atom,

G is selected from **the group consisting of** hydrogen, C_3-C_8-cycloalkyl, methoxycarbonyl, tert-butoxycarbonyl, benzyloxycarbonyl, trifluoroacetyl, diphenylphosphinoyl,

$$-(CH_2)_r-(CR^{13}R^{14})_s-R^{12} \qquad [(G1)],$$

$$-\overset{\overset{O}{\|}}{C}-(CH_2)_r-(CR^{13}R^{14})_s-R^{12} \qquad [(G2a)],$$

$$-\overset{\overset{O}{\|}}{C}-(CH_2)_r-NR^{12}R^{14} \qquad [(G2b)],$$

and

$$-SO_2-(CH_2)_rR^{12} \qquad [(G3)],$$

wherein

r is 0, 1 or 2,

s is 0 or 1,

R^{12} is selected from **the group consisting of** hydrogen, methyl, benzyl, phenyl, [the group consisting of] indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, flourenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and oxodibenzocycloheptenyl, dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl bound directly or over a

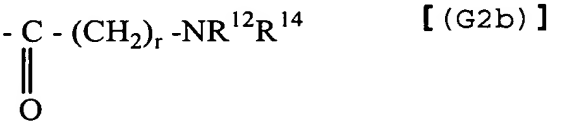
methylene group, [and the group consisting of] furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl, dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolinyl, benzisoxazolyl, oxobenzisoxazolinyl, benzothiazolyl, oxobenzthiazolinyl, benzoisothiazolyl, oxobenzoisothiazolinyl, benzimidazolyl, oxobenzimidazolinyl, benzofurazanyl, benzothiadiazolyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl, pyrazolopyridyl, thienopyrimidinyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, dihydroquinolyl, oxodihydroquinolinyl, tetrahydroquinolyl, oxotetrahydroquinolinyl, benzodioxanyl, quinoxalinyl, quinazolinyl, naphthyridinyl, carbazolyl, tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, oxobenzocycloheptathienyl, dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, dihydropyridobenzoxepinyl, dihydrodibenzothiazepinyl, and oxodihydrodibenzothiazepinyl, bound directly or over a methylene group,

R^{13} is selected from **the group consisting of** hydrogen, methyl, benzyl and phenyl,

R^{14} is selected from **the group consisting of** hydrogen,

hydroxy, methyl, benzyl, phenyl, [and the group consisting of] naphthyl, furyl, thienyl, oxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in formula



[(G2b)]

$-NR^{12}R^{14}$ [optionally is] may be selected from **the group consisting of** pyrrolidine, piperidine, (1H)-tetrahydropyridine, hexahydroazepine, octahydroazocine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, 2-azabicyclo[2.2.1]heptane, 7-azabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, 8-azabicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indol, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine and (5H)-tetrahydrodibenzazocine,

wherein aromatic [ring systems are optionally] **rings are** substituted **or unsubstituted** independently of each other by

one to three substituents independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, **and a substituted** C_1-C_6-alkoxy entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups [in the ring] **of an aromatic ring in the substituted C1-C6 alkoxy** [or ring system optionally] form an additional ring over a methylenedioxy bridge.

45. (once amended) A compound according to claim 22, wherein

R^1 is selected from **the group consisting of** hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and hydroxy,

R^2 and
R^3 are hydrogen,

R^4 is hydrogen or hydroxy,

k is 0 or 1,

A is **selected from the group consisting of** C_2-C_4-alkenylene,

[or] 1,3-butadienylene, [which are optionally] **a C_2-C_4-alkenylene** substituted by fluorine, **and a 1,3-butadienylene substituted by fluorine,**

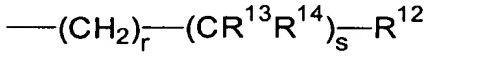
D is selected from **the group consisting of** C_2-C_6-alkylene, C_2-C_6-alkenylene,

C_2-C_6-alkylene and C_2-C_6-alkenylene wherein the double bond [optionally] is to ring E, and

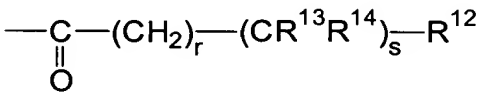
an isosterically replaced C2 to C6 group selected from the group consisting of C_2-C_6-alkylene and C_2-C_6-alkenylene, [wherein] **the isosterically replaced C2 to C6 group having** a methylene unit **which** is isosterically replaced by O, NH, $N(CH_3)$ or CO, or an ethylene group **which** is isosterically replaced by NH-CO or CO-NH, or a propylene group **which** is isosterically replaced by NH-CO-O or O-CO-NH,

E is **selected from the group consisting of** piperidine, **and a substituted piperidine** wherein the heterocyclic ring [optionally] is substituted by an oxo group adjacent to the nitrogen atom,

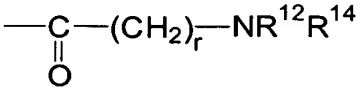
G is selected from **the group consisting of** hydrogen, tert-butoxycarbonyl, diphenylphosphinoyl,



(G1),



(G2a),



(G2b),

and

$$—SO_2—(CH_2)_r R^{12} \qquad (G3)$$

wherein

r is 0 or 1,

s is 0 or 1,

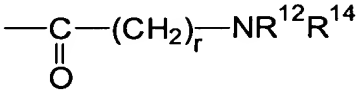
R^{12} is selected from **the group consisting of** hydrogen, methyl, benzyl, phenyl, [the group consisting of] indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and dihydrodibenzocycloheptenyl, bound directly or over a methylene group, [and the group consisting of] furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolinyl, benzothiazolyl, oxobenzthiazolinyl, benzimidazolyl, oxobenzimidazolinyl, benzofurazanyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolinyl, tetrahydroquinolyl, oxotetrahydroquinolinyl, benzodioxanyl, quinazolinyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and

dihydrodibenzothiazepinyl, bound directly or over a methylene group,

R^{13} is selected from **the group consisting of** hydrogen, methyl, benzyl and phenyl,

R^{14} is selected from **the group consisting of** hydrogen, hydroxy, methyl, benzyl, phenyl, [and the group consisting of] naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in the formula



(G2b)

$-NR^{12}R^{14}$ [optionally is] **may be** selected from pyrrolidine, piperidine, hexahydroazepine, morpholine, 2,5-diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-dihydrodibenzo[b,e]oxazepine and (11H)-dihydrodibenzo[b,e]thiazepine,

wherein aromatic **rings** [ring systems optionally] are substituted **or unsubstituted**, independently of each other, by one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl,

trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, **a substituted** C_1-C_6-alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups on the aromatic ring or ring system **may** [optionally] form an additional ring over a methylenedioxy bridge.

46. (once amended) A compound according to claim 45, wherein:

R^1 is selected from **the group consisting of** hydrogen, fluorine, methyl, trifluoromethyl and hydroxy,

R^2 and

R^3 are hydrogen,

R^4 is hydrogen or hydroxy,

k is 0,

A is ethenylene or 1,3-butadienylene

D is **selected from the group consisting of** C_2-C_6-alkylene, [or] C_2-C_6-alkenylene, **a C_2-C_6-alkylene** wherein the double bond [optionally] is to ring E, **and a C_2-C_6-alkenylene wherein the double bond is to ring E,**

E is selected from **the group consisting of** pyrrolidine, piperidine, hexahydroazepine and morpholine,

G is selected from **the group consisting of** benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl,

furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenyl-thienylmethyl, phenyl-pyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolinyl-1-carbonyl, dihydrodibenzazepin-N-carbonyl, tetrahydroquinolinyl-N-carbonyl, tetrahydrobenzo[b]azepinyl-N-carbonyl, methanesulfonyl, phenylsulfonyl, p-toluenesulfonyl, naphthylsulfonyl, quinolinsulfonyl, and diphenylphosphinoyl,

wherein aromatic **rings** [ring systems optionally] are substituted **or unsubstituted** independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, C_1-C_6-alkoxy, entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups in the ring or ring system **may** [optionally] form an additional ring over a methylenedioxy bridge.

47. (once amended) A compound according to claim 4, which is selected from **the group consisting of**

N-[4-(1-methylsulfonylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(1-naphthylaminocarbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, and

N-[4-(1-diphenylphosphinoyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide

or as a pharmaceutically acceptable acid addition salt thereof.

48. (once amended) A compound according to claim 42, which is selected from **the group consisiting of** N-[4-(1-acetylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-[4-(1-diphenylacetyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(3,3-diphenylpropionyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-

pentadienoic acid amide, and N-{4-[1-(9-oxo-9H-fluoren-4-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

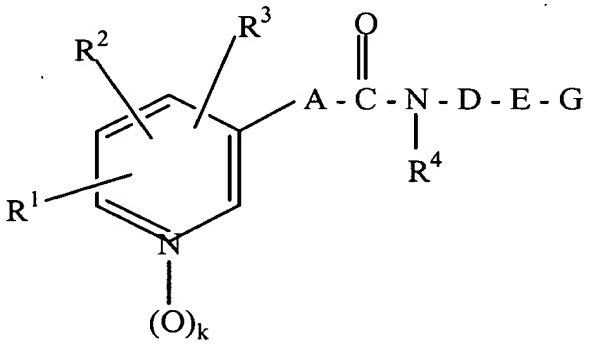
49. (once amended) A compound according to claim 42, which is selected from **the group consisting of** N-{4-[1-(phenylpyridin-3-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(phenylpyridin-4-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide and N-{4-[1-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

50. (once amended) A compound according to claim 42, which is selected from **the group consisting of** N-[7-(1-diphenylmethylpiperidin-4-yl)-heptyl]-3-(pyridin-3-yl)-acrylamide, N-[8-(1-diphenylmethylpiperidin-4-yl)-octyl]-3-(pyridin-3-yl)-acrylamide, N-[3-(1-diphenylmethylpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide, and N-[3-(1-benzylpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide or as a pharmaceutically acceptable acid addition salt thereof.

51. (once amended) A compound according to claim 42, which is selected from **the group consisting of** N-[2-(1-diphenylmethylpiperidin-4-yl)-ethyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[4-(1-diphenylmethylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[5-(1-diphenylmethylpiperidin-4-yl)-pentyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide and N-[6-(1-diphenylmethylpiperidin-4-yl)-hexyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide or as a pharmaceutically acceptable

acid addition salt thereof.

56. (once amended) A pharmaceutical composition comprising one or more of the compounds according to **formula (I)** [claim 42 as active ingredient, optionally together with one or more pharmaceutically acceptable carriers, one or more toxicologically safe adjuvants, and optionally in combination with one or more other active ingredients] **and pharmaceutically acceptable salts of formula (I)**



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, C_1-C_4-hydroxyalkyl, hydroxy, C_1-C_4-alkoxy, benzyloxy, C_2-C_4-alkanoyloxy, C_1-C_4-alkylthio, C_2-C_5-alkoxycarbonyl, aminocarbonyl, C_3-C_9-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6, and bridged R^1R^2; wherein

R^5 is selected from the group consisting of hydrogen and C_1-C_6-alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6-alkyl, trifluoromethyl and hydroxy and bridged R^1R^2;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6-alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6-alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, C_3-C_6-alkenyl, hydroxy, C_1-C_6-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6-alkenylene,

a substituted C_2-C_6-alkenylene which is substituted one to three-fold by C_1-C_3-alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6-alkadienylene,

a substituted C_4-C_6-alkadienylene which is substituted once or twice by C_1-C_3-alkyl, fluorine, cyano, or phenyl,

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3-alkyl, fluorine, or cyano, and ethinylene;

D is selected from the group consisting of

C_1-C_{10}-alkylene,

a substituted C_1-C_{10}-alkylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

C_2-C_{10}-alkenylene,

a substituted C_2-C_{10}-alkenylene which is substituted once

or twice by C_1-C_3-alkyl or hydroxy,

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy, wherein the double bond is to E,

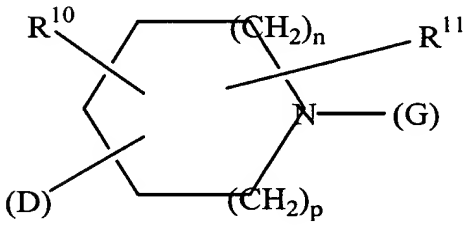
C_3-C_{10}-alkinylene,

a substitued C_3-C_{10}-alkinylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1-C_{10}-alkylene, C_2-C_{10}-alkenylene and C_3-C_{10}-alkinylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, **NR^9**, CO, SO or SO_2; wherein

R^9 is selected from the group consisting of hydrogen, C_1-C_3-alkyl, C_2-C_6-acyl and methanesulfonyl;

E is



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wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3 wherein **n + p** $\leq$ 3,

R^{10} is selected from the group consisting of hydrogen, C_1-C_3-alkyl, hydroxy, hydroxymethyl, carboxy and C_2-C_7-alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen

and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, **G1**, **G2**, **G3**, **G4** and **G5**; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of

hydrogen,

C_1-C_6-alkyl,

C_3-C_6-alkenyl,

C_3-C_6-alkinyl,

C_3-C_8-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond

which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R^{13} has the same meaning as R^{12}, but is selected independently thereof;

R^{14} is selected from the group consisting of hydrogen,

hydroxy,

methyl,

benzyl,

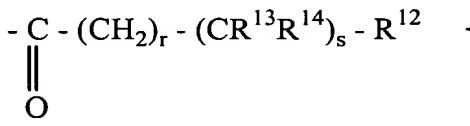
phenyl,

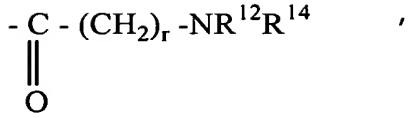
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

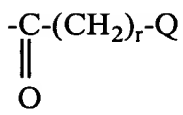
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



;

wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

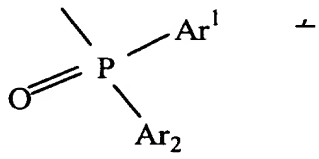
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-SO_2-(CH_2)_r-R^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-COR^{15}$,

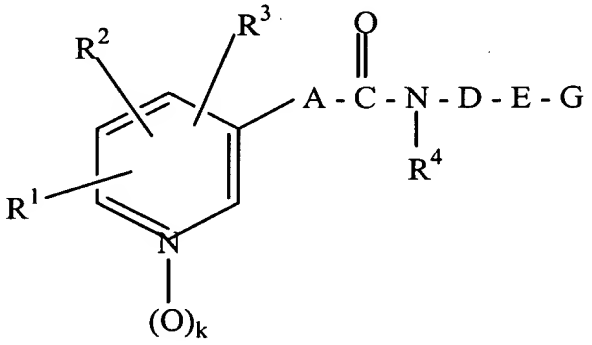
wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1-C_6-alkoxy, C_3-C_6-alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, and a substituted C_1-C_6-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C_1-C_6 alkoxy may form an additional ring over a methylenedioxy bridge,

wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

64. (once amended) A method of **inhibiting tumor cell growth** [treating cancer] in **a** [the] human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition [of claim 56] **, wherein the pharmaceutical composition includes a compound of general formula (I)**



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, C_1-C_4-hydroxyalkyl, hydroxy, C_1-C_4-alkoxy, benzyloxy, C_2-C_4-alkanoyloxy, C_1-C_4-alkylthio, C_2-C_5-alkoxycarbonyl, aminocarbonyl, C_3-C_9-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6, and bridged R^1R^2; wherein

R^5 is selected from the group consisting of hydrogen and C_1-C_6-alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6-alkyl, trifluoromethyl and hydroxy and bridged R^1R^2;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6-alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6-alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, C_3-C_6-alkenyl, hydroxy, C_1-C_6-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6-alkenylene,

a substituted C_2-C_6-alkenylene which is substituted one to three-fold by C_1-C_3-alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6-alkadienylene,

a substituted C_4-C_6-alkadienylene which is substituted once or twice by C_1-C_3-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3-alkyl, fluorine, or cyano, and ethinylene;

D is selected from the group consisting of

C_1-C_{10}-alkylene,

a substituted C_1-C_{10}-alkylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

C_2-C_{10}-alkenylene,

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy, wherein the double bond is to E,

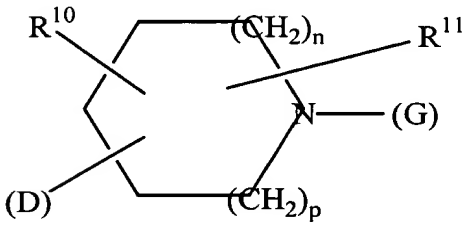
C_3-C_{10}-alkinylene,

a substitued C_3-C_{10}-alkinylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1-C_{10}-alkylene, C_2-C_{10}-alkenylene and C_3-C_{10}-alkinylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, **NR^9**, CO, SO or SO_2; wherein

R^9 is selected from the group consisting of hydrogen, C_1-C_3-alkyl, C_2-C_6-acyl and methanesulfonyl;

E is



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wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3 wherein **n + p** $\leq$ 3,

R^{10} is selected from the group consisting of hydrogen, C_1-C_3-alkyl, hydroxy, hydroxymethyl, carboxy and C_2-C_7-alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, **G1**, **G2**, **G3**, **G4** and **G5**; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of

hydrogen,

C_1-C_6-alkyl,

C_3-C_6-alkenyl,

C_3-C_6-alkinyl,

C_3-C_8-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring, and

either directly or over a methylene group;

R^{13} has the same meaning as R^{12}, but is selected independently thereof;

R^{14} is selected from the group consisting of hydrogen,

hydroxy,

methyl,

benzyl,

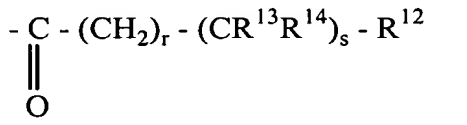
phenyl,

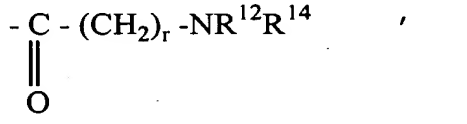
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

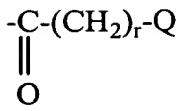
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



;

wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

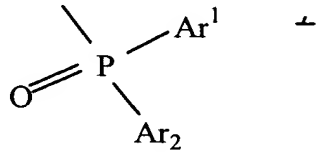
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-SO_2-(CH_2)_r-R^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

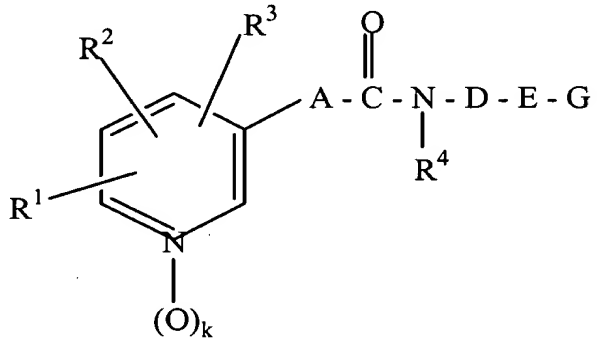
G5 is $-COR^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1-C_6-alkoxy, C_3-C_6-alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, and a substituted C_1-C_6-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C_1-C_6 alkoxy may form an additional ring over a methylenedioxy bridge.

65. (Once amended) A method of suppressing **autoimmune disease** [immunoreactions] in [the] **a** human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition of [claim 56], wherein the pharmaceutical composition includes a compound of general formula (I) or a pharmaceutically acceptable salt of formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, C_1-C_4-hydroxyalkyl, hydroxy, C_1-C_4-alkoxy, benzyloxy, C_2-C_4-alkanoyloxy, C_1-C_4-alkylthio, C_2-C_5-alkoxycarbonyl, aminocarbonyl, C_3-C_9-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR^5R^6, and bridged R^1R^2; wherein

R^5 is selected from the group consisting of hydrogen and C_1-C_6-alkyl; and

R^6 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6-alkyl, trifluoromethyl and hydroxy and bridged R^1R^2;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6-alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6-alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6-alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6-alkyl, C_3-C_6-alkenyl, hydroxy, C_1-C_6-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6-alkenylene,

a substituted C_2-C_6-alkenylene which is substituted one to three-fold by C_1-C_3-alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6-alkadienylene,

a substituted C_4-C_6-alkadienylene which is substituted once or twice by C_1-C_3-alkyl, fluorine, cyano, or phenyl,

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3-alkyl, fluorine, or cyano, and ethinylene;

D is selected from the group consisting of

C_1-C_{10}-alkylene,

a substituted C_1-C_{10}-alkylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

C_2-C_{10}-alkenylene,

a substituted C_2-C_{10}-alkenylene which is substituted once

or twice by C_1-C_3-alkyl or hydroxy,

a substituted C_2-C_{10}-alkenylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy, wherein the double bond is to E,

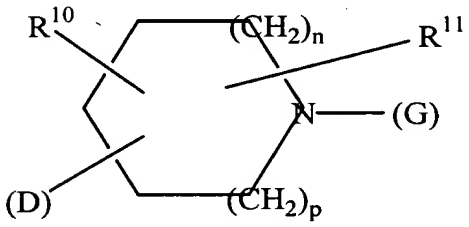
C_3-C_{10}-alkinylene,

a substitued C_3-C_{10}-alkinylene which is substituted once or twice by C_1-C_3-alkyl or hydroxy,

an isosterically replaced C_1 to C_{10} group selected from the group consisting of C_1-C_{10}-alkylene, C_2-C_{10}-alkenylene and C_3-C_{10}-alkinylene, the isosterically replaced C_1 to C_{10} group having methylene units and one to three of the methylene units are isosterically replaced by O, S, **NR^9**, CO, SO or SO_2; wherein

R^9 is selected from the group consisting of hydrogen, C_1-C_3-alkyl, C_2-C_6-acyl and methanesulfonyl;

E is



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wherein **n** and **p** are, independent of each other, 0, 1, 2, or 3 wherein **n + p** $\leq$ 3,

R^{10} is selected from the group consisting of hydrogen, C_1-C_3-alkyl, hydroxy, hydroxymethyl, carboxy and C_2-C_7-alkoxycarbonyl;

R^{11} is selected from the group consisting of hydrogen

and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen, **G1**, **G2**, **G3**, **G4** and **G5**; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of

hydrogen,

C_1-C_6-alkyl,

C_3-C_6-alkenyl,

C_3-C_6-alkinyl,

C_3-C_8-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles which heterocycles contain one to three hetero-atoms selected from the group consisting of N, S and O, which heterocycles are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond

which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R^{13} has the same meaning as R^{12}, but is selected independently thereof;

R^{14} is selected from the group consisting of hydrogen,

hydroxy,

methyl,

benzyl,

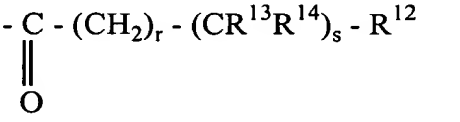
phenyl,

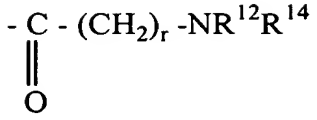
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

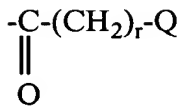
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



;

wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

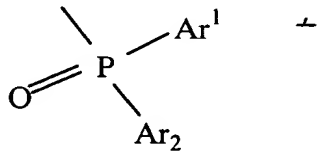
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-SO_2-(CH_2)_r-R^{12}$,

G4 is



wherein

Ar^1 is selected from the group consisting of phenyl, pridyl and naphthyl; and

Ar^2 is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is $-COR^{15}$,

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1-C_6-alkoxy, C_3-C_6-alkenyloxy and benzyloxy; and

wherein aromatic rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 are unsubstituted or substituted, the substituted rings in R^1, R^4, R^{12}, R^{13}, R^{14}, R^{15}, Q, Ar^1 and Ar^2 having one to three substituents which are independently selected from the group consisting of halogen, cyano, C_1-C_6-alkyl, trifluoromethyl, C_3-C_8-cycloalkyl, phenyl, benzyl, hydroxy, C_1-C_6-alkoxy, C_1-C_6-alkoxy, and a C_1-C_6 alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C_1-C_6-alkylthio, carboxy, C_1-C_6-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C_1-C_6-alkylamino, and di-(C_1-C_6-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C_1-C_6 alkoxy may form an additional ring over a methylenedioxy bridge.